March 29, 2024

Haemonetics Corporation
Julie Bergeman
Senior Regulatory Affairs Specialist
125 Summer St
Boston, Massachusetts 02110

Re: K232018
Trade/Device Name: Citrated: K, KH, RTH, FFH
Regulation Number: 21 CFR 864.5425
Regulation Name: Multipurpose System For In Vitro Coagulation Studies
Regulatory Class: Class II
Product Code: JPA
Dated: July 6, 2023
Received: July 7, 2023

Dear Julie Bergeman:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device"

(https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Min Wu -S

Min Wu, Ph.D.
Branch Chief
Division of Immunology and Hematology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K232018

Device Name
Citrated: K, KH, RTH, FFH

Indications for Use *(Describe)*
The TEG 6s Hemostasis System consists of the TEG 6s Hemostasis Analyzer and the Citrated: K, KH, RTH, FFH assay cartridge. The TEG 6s Hemostasis System is intended for in vitro diagnostic use with adult patients where an evaluation of their blood hemostasis properties is desired. The TEG 6s Hemostasis System records the kinetic changes in a sample of 3.2% citrated whole blood as the sample clots and provides semi-quantitative results. The TEG 6s Hemostasis System can be used in the laboratory or at the point-of-care.

The Citrated: K, KH, RTH, FFH assay cartridge is intended to be used in patients where heparin/heparinoids may be present and who are at an increased risk of coagulopathy. Hemostasis evaluations are indicated to assess clinical conditions in cardiovascular surgery, cardiovascular procedures (e.g. minimally invasive valve replacement or repairs) and liver transplantation to assess hemorrhage or thrombosis conditions before, during and following the procedure.

The Citrated: K, KH, RTH, FFH assay cartridge contains four independent assays (CK, CKH, CRTH and CFFH) and the system output consists of a table of numerical values for parameters R, MA, and LY30.

The CK assay monitors the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. Clotting characteristics are described by the functional parameters R (clotting time) and MA (maximum clot strength).

The CKH assay monitors the effects of heparin in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. CKH is used in conjunction with CK, and heparin influence is determined by comparing Clotting Times (R) between the two tests. LY30 describes fibrinolysis 30 minutes after reaching maximum clot strength.

The CRTH assay monitors the hemostasis process after stimulation of both the intrinsic and extrinsic pathways in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (maximum clot strength with contributions of both platelets and fibrin).

The CFFH assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s Hemostasis System after blocking platelet contributions to clot strength, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (fibrinogen contribution to maximum clot strength).

Results from the TEG 6s analysis should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests.

For professional use only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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HAEMONETICS®

510(k) Summary

Submitter: Haemonetics Corporation
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Date Prepared: March 26, 2024

1. Device Information

Device Trade Name: Citrated: K, KH, RTH, FFH
Common Name: Whole Blood Hemostasis System
Classification Name: System, Multipurpose For In Vitro Coagulation Studies
Regulatory Class: 2
Regulation Number: 21 CFR 864.5425
Product Code: JPA

2. Legally Marketed Predicate Device

Predicate #	Predicate Trade Name	Product Code
K150041	TEG 6s with the Citrated Multichannel Cartridge	JPA

3. Device Description Summary

TEG® 6s System Description

The TEG® 6s Hemostasis System (TEG® hemostasis analyzer and TEG® 6s assay cartridges) is intended for in vitro diagnostic use to provide semi-quantitative indications of a blood sample's ability to form and maintain a clot. The TEG® 6s Hemostasis System records the kinetic changes in a sample of whole blood as the sample clots, retracts and/or lyses. The system output consists of a table of numerical values and graphs resulting from the hemostasis process over time. This information can be used by clinicians to aid in determining if a clotting dysfunction or coagulopathy is present.

To perform a test, a disposable TEG® 6s assay cartridge is inserted into the TEG® 6s hemostasis analyzer. The instrument reads the bar code on the cartridge and identifies the type of cartridge for operator confirmation. Blood (collected in a 3.2% sodium citrate tube) or Quality Control (QC) material is added to the entry port on the cartridge and drawn into the cartridge under the TEG® 6s hemostasis analyzer control. The amount of the sample drawn into the cartridge is determined by the pre-set volume of the blood chambers in the cartridge. Once in the cartridge, the sample is metered into as many as 4 separate analysis channels, depending upon the assays being performed. Reconstitution of reagents dried within the cartridge is accomplished by moving the sample back and forth through reagent chambers, under the control of microfluidic valves and bellows (pumps) within the cartridge. After each sample has been mixed with reagent, it is delivered to a test cell where it is monitored for viscoelastic changes due to coagulation. Excess sample material is moved under microfluidic control into an enclosed waste chamber within the cartridge.

TEG® 6s Measurement Technique

The TEG® 6s technology is based on a disposable cartridge containing up to 4 independent measurement cells. Each cell consists of a short vertically-oriented injection molded tube (ring). Detection of clotting in the TEG® 6s Hemostasis System is performed optically. A piezoelectric actuator vibrates the measurement cell(s) through a motion profile composed of summed sinusoids at different frequencies. The movement of the measurement cells will induce motion in the sample meniscus, which will be detected by a photodiode. The resulting motion of the meniscus is monitored optically and analyzed by the instrument to calculate the resonant frequency and modulus of elasticity (stiffness) of the sample. By performing a Fast Fourier Transform (FFT) on meniscus motion data, the resonant frequencies can be determined. The analyzer monitors the harmonic motion of a hanging drop of blood in response to external vibration. As the sample transitions from a liquid state to a gel-like state during clotting, the modulus of elasticity (stiffness) and therefore resonant frequency increase. The TEG® 6s hemostasis analyzer measures these variations in resonant frequency during clotting and lysis.

Resonance is the tendency of a material or structure to oscillate with greater amplitude at some frequencies than others. The exact frequencies at which resonance occurs will depend on the stiffness and mass of the sample. Stiffness, in turn, is a function of a material's modulus of elasticity and the boundary conditions to which the material is exposed, such as the geometry and materials of a test cell. By holding these boundary conditions and sample mass constant from sample to sample, the TEG® 6s Hemostasis System allows direct comparison of

elasticity between samples. The output measurements are displayed in a table and on a graphical tracing that reflects the hemostasis profile of the clot formation.

In a typical test, blood that has been delivered to the measurement cell will not clot for several minutes. During this time the sample has no inherent stiffness except that provided by surface tension, and since this remains constant the measured resonant frequencies will not change.

Once clotting begins, however, the elastic modulus and thus the resonant frequencies increase rapidly. During fibrinolysis, the process is reversed, with elastic modulus and resonant frequencies decreasing. In tests where clotting does not occur, the resonant frequency of the sample will not change. During coagulation, however, a clot will bind to the ring contained in the cartridge and the resonant frequency will rise with increasing firmness of the clot. The TEG® 6s hemostasis analyzer collects meniscus motion data, tracks changing resonant frequencies and analyzes the frequency data to provide semi-quantitative parameters describing the clot.

The TEG® 6s Hemostasis System monitors the interaction of platelets within the fibrin mesh of the clot during clot formation and lysis, all in a whole-blood setting. The TEG® 6s Hemostasis System uses thromboelastography to provide continuous measurement of clot elasticity.

Method Comparison testing has been performed, yielding data from 8 clinical sites. These data include the applicable parameters for the tests in the Citrated: K, KH, RTH, FFH assay cartridge. Table 1 provides the definitions that apply to calculated parameters in the TEG® 6s Hemostasis System.

Table 1. TEG® 6s parameter definitions

TEG® 6s Parameter	Definition	Parameter Relation to Hemostasis
R	R is the time from the start of the test until initial fibrin formation. This represents the enzymatic portion of coagulation.	Normal / reduced / increased speed of coagulation initiation
MA	MA, or Maximum Amplitude, represents the maximum firmness of the clot during the test.	Normal / reduced / increased clot elasticity/strength
LY30	LY30 is a measurement of the rate of fibrinolysis 30 minutes after MA is reached. The LY30 measurement is based on the reduction of the tracing area that occurs between the time that M A is measured until 30 minutes after the MA is	Normal / reduced clot stability; clot dissolution

	defined.	

Citrated Assays

Citrated Kaolin (CK) assay

The CK assay is a semi-quantitative in vitro diagnostic assay for monitoring the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG® 6s Hemostasis System. The CK assay consists of Kaolin which is used in the assay for activation of coagulation. It is combined with calcium chloride to neutralize the sodium citrate used to anticoagulate the blood sample.

The clotting characteristics of the CK generated hemostasis profile are described by the functional parameters Clotting Time (R) and Maximum Clot strength (MA). Since it may take an hour or more for a non-activated whole blood sample to reach maximum amplitude MA, Kaolin is essential to reduce run time and variability associated with running non-activated whole blood samples.

Citrated Kaolin with Heparinase (CKH) assay

The CKH assay is a semi-quantitative in vitro diagnostic assay for monitoring the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG® 6s Hemostasis System. CKH is used in conjunction with CK, and heparin influence is determined by comparing Clotting Times (R) between the two tests. LY30 describes fibrinolysis 30 minutes after reaching maximum clot strength. The Kaolin with heparinase assay neutralizes the anticoagulant property of heparin. Calcium Chloride ($CaCl_2$) is included to neutralize any sodium citrate in the blood.

The CKH assay monitors the effects of heparin, a commonly used anticoagulant in surgical procedures. Even very low concentrations of heparin, fractions of IU/mL of blood, can noticeably increase the R time and can even completely anticoagulate the blood, making it difficult if not impossible to monitor developing coagulopathies that are masked by high levels of therapeutic heparin.

Citrated RapidTEG™ with Heparinase (CRTH) assay

The CRTH assay is a semi-quantitative in vitro diagnostic assay that monitors the hemostasis process after stimulation of both the intrinsic and extrinsic pathways in 3.2% citrated whole blood specimens on the TEG® 6s Hemostasis System, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter: MA (maximum clot strength with contributions of both platelets and fibrin). The CRTH assay produces an

accelerated clotting time which allows for an earlier MA result compared to the CK assay. Therefore, in the TEG® Hemostasis System, the CRTH assay is simultaneously run along with the CK and CKH assays to provide a fast way to reach a stable value for MA (CRTH) while still measuring the time- dependent parameters (CK).

As described in the CK assay, Kaolin is used for activation of coagulation and is combined with Calcium Chloride to neutralize sodium citrate in the blood sample. The addition of Tissue Factor is used for coagulation activation that would be classically described as extrinsic. The addition of heparinase in the assay cartridge neutralizes the effects of heparin in the sample. The CRTH hemostasis profile resulting from Kaolin and Tissue Factor activation provides a measure of the strength of the clot and the breakdown of the clot, or fibrinolysis.

Citrated Functional Fibrinogen with Heparinase (CFFH) assay

The CFFH assay is a semi-quantitative in vitro diagnostic assay for monitoring the hemostasis process after blocking platelet contributions to clot strength in 3.2 % citrated whole blood specimens, neutralizing the effect of heparin in the sample. The CFFH assay consists of Tissue Factor and abciximab. It is combined with Calcium Chloride to neutralize sodium citrate in the blood sample. The addition of heparinase in the assay cartridge neutralizes the effects of heparin in the sample. Tissue Factor is used for coagulation activation that would be classically described as extrinsic, with platelet aggregation inhibited by abciximab (a GPIIb/IIIa inhibitor), excluding its contribution to clot strength, and thereby measuring fibrinogen contribution to clot strength.

The Clotting characteristics are described by the functional parameter: MA (fibrinogen contribution to maximum clot strength) and measures the part of clot strength that is contributed by fibrinogen in the blood sample.

4. Intended Use/Indications for Use

The TEG 6s Hemostasis System consists of the TEG 6s Hemostasis Analyzer and the Citrated: K, KH, RTH, FFH assay cartridge. The TEG 6s Hemostasis System is intended for in vitro diagnostic use with adult patients where an evaluation of their blood hemostasis properties is desired. The TEG 6s Hemostasis System records the kinetic changes in a sample of 3.2% citrated whole blood as the sample clots and provides semi-quantitative results. The TEG 6s Hemostasis System can be used in the laboratory or at the point-of-care.

The Citrated: K, KH, RTH, FFH assay cartridge is intended to be used in patients where heparin/heparinoids may be present and who are at an increased risk of coagulopathy. Hemostasis evaluations are indicated to assess clinical conditions in cardiovascular surgery, cardiovascular procedures (e.g. minimally invasive valve replacement or repairs) and liver transplantation to assess hemorrhage or thrombosis conditions before, during and following the procedure.

The Citrated: K, KH, RTH, FFH assay cartridge contains four independent assays (CK, CKH, CRTH and CFFH) and the system output consists of a table of numerical values for parameters R, MA, and LY30.

The CK assay monitors the hemostasis process via the intrinsic pathway in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. Clotting characteristics are described by the functional parameters R (clotting time) and MA (maximum clot strength).

The CKH assay monitors the effects of heparin in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System. CKH is used in conjunction with CK, and heparin influence is determined by comparing Clotting Times (R) between the two tests. LY30 describes fibrinolysis 30 minutes after reaching maximum clot strength.

The CRTH assay monitors the hemostasis process after stimulation of both the intrinsic and extrinsic pathways in 3.2% citrated whole blood specimens on the TEG 6s Hemostasis System, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (maximum clot strength with contributions of both platelets and fibrin).

The CFFH assay monitors hemostasis of 3.2% citrated whole blood specimens in the TEG 6s Hemostasis System after blocking platelet contributions to clot strength, neutralizing the effect of heparin in the sample. Clotting characteristics are described by the functional parameter MA (fibrinogen contribution to maximum clot strength).

Results from the TEG 6s analysis should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests.

For professional use only.

5. Comparison Citrated: K, KH, RTH, FFH and predicate device

Indications for Use Comparison

The TEG® 6s Hemostasis System consists of the TEG® 6s hemostasis analyzer including analyzer software and assay cartridges. The assay cartridges predicate device is the K150041 TEG 6s with the Citrated Multichannel Cartridge (07-601-US). The indications for use are of the same intent with the following inclusions:

1. Heparinase is included in the RT and FF channels of the new assay cartridge.
2. Use location is defined as laboratory and point-of-care for the new assay cartridge.
3. Patient types are defined for the new assay to include the same population as the predicate (cardiovascular surgery, cardiology procedures) with expansion to patients undergoing liver transplant.

Technology Comparison

Substantial equivalence is being demonstrated through a method comparison clinical study. No key design elements required changes for the cartridge including the reagent spotting technology, the microfluidic pathway, the shaker design, or the cartridge interface with the analyzer. The reagent channel order has been rearranged; however, that has been shown to not influence cartridge functionality. There is no change to the design of the cartridge and there is no change in the mechanics of how the cartridge is run on the TEG® 6s hemostasis analyzer. No additional product development of the TEG® 6s analyzer hardware and TEG® 6s software was required to add the Citrated: K, KH, RTH, FFH assay cartridge.

Table-2 Summary of Technological Characteristics for Substantial Equivalence: Similarities

Item	***K150041 TEG 6s with the Citrated Multichannel Cartridge (Predicate)***	***Citrated: K, KH, RTH, FFH***
Analyzer		
Technological Purpose	Monitoring the physical response of a clot to low levels of applied strain (resonance frequency)	Same
Measurement	Changes in physical clot elasticity over time	Same
Matrix	3.2% citrated whole blood	Same
Initial Warm Up Time	5 minutes	Same

Item	*K150041 TEG 6s with the Citrated Multichannel Cartridge (Predicate)*	*Citrated: K, KH, RTH, FFH*
Analyzer-Hardware	Fully integrated Thromboelastography analyzer	Same
Analyzer-Measuring Technique	Non-contact optical measurement of shear elasticity of a coagulating sample	Same
Measurement Output	Graphical tracings of resonant frequency per reagent type; table of parameters	Same
Assay and Reagents		
Assays	CK, CKH, CRT, CFF	CK, CKH, CRTH, CFFH Same with inclusion of heparinase for the CRT and CFF channels
Assay Reagents	CK – kaolin and $CaCl_2$ CKH – kaolin and $CaCl_2$ with heparinase CRT – tissue factor, kaolin and $CaCl_2$ CFF – abciximab, tissue factor and $CaCl_2$	Same with inclusion of heparinase for the CRT and CFF channels
Assay Parameters Reported	CK: R, K, Angle, MA CKH: R CRT: MA CFF: MA, FLEV	CK: R, MA CKH: R, LY30 CRTH: MA CFFH: MA
Quality Controls	Cartridge Reagent QC - Level 1 Cartridge Reagent QC - Level 2	Same

Table-3 Summary of Technological Characteristics for Substantial Equivalence: Differences and Clinical Value Comparisons

Item	*K150041 TEG 6s with the Citrated Multichannel Cartridge (Predicate)*	*Citrated: K, KH, RTH, FFH*
Use Location	N/A	The TEG® 6s Hemostasis System with Citrated: K, KH, RTH, FFH assay cartridge can be used in the laboratory or at the point-of-care.
Patient Population from Intended Use	Hemostasis evaluations are commonly used to assess clinical conditions in cardiovascular surgery and cardiology procedures to assess hemorrhage or thrombosis	The Citrated: K, KH, RTH, FFH assay cartridge is intended to be used in patients where heparin/heparinoids may be present and who are at an increased risk of coagulopathy. Hemostasis

	conditions before, during and following the procedure.	evaluations are indicated to assess clinical conditions in cardiovascular surgery, cardiovascular procedures (e.g. minimally invasive valve replacement or repairs) and liver transplantation to assess hemorrhage or thrombosis conditions before, during and following the procedure.
Clinical Value Comparisons		
Clinical Value of Citrated: Kaolin (CK) Parameter R (min)	Initiation phase of coagulation triggered by enzymatic clotting factors and culminating with the initial fibrin formation. A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies or heparin.	Kaolin R is the time in minutes elapsing between sample activation and the point in time where clotting provides enough resistance to produce a 2 mm amplitude reading on the TEG analyzer tracing. The CK - R parameter represents the initiation phase of coagulation triggered by enzymatic clotting factors and culminating with the initial fibrin formation. A prolonged R value is indicative of slow clot formation, and a shortened R value is indicative of fast clot formation. *Clinical Value*. A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies, heparin, or other anticoagulants.
Clinical Value of Citrated: Kaolin (CK) Parameter MA (mm)	MA, or Maximum Amplitude, represents the maximum firmness of the clot during the test. The MA provides information about the contribution of platelets/fibrin to the overall strength of the clot.	The maximal strength of the clot when activated with kaolin. This represents the combination of the contribution of fibrinogen and platelets to clot strength. *Clinical Value:* The MA provides information of platelets and fibrinogen to the overall clot strength without excluding the influence of heparin. A decreased MA is indicative of low clot strength, which could be due to decreased platelet contribution or decreased fibrinogen; whereas, an increased MA is indicative of high clot strength, which could be due to increased platelet or fibrinogen contribution.

Clinical Value of Citrated: Kaolin with Heparinase (CKH) Parameter R (min) Heparinase is included in the predicate and subject device	Initiation phase of coagulation triggered by enzymatic coagulation factors and culminating with the initial fibrin formation. A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies or heparin. Inclusion of heparinase in the blood chamber channel of the cartridge provides ability to compare R (min) without the effect of heparin on the clot.	The reaction time between initiation of the clot (via kaolin) and the point where the tracing reaches 2mm of amplitude, with heparinase being used to neutralize the effect of heparin. *Clinical Value:* A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies or non-heparin anticoagulant. A shortening of the CKH-R compared to the CK-R indicates effect of heparin in the blood sample.
Clinical Value of Citrated: Kaolin with Heparinase (CKH) Parameter LY30 (%)	Parameter LY30 (%) is not reported for the predicate device.	Clot lysis, in a sample with heparinase to neutralize effects of heparin, expressed as a percent reduction in clot strength 30 minutes after the MA is reached. *Clinical Value:* LY30 provides information about fibrinolytic activity.
Clinical Value of Citrated: RapidTEG with Heparinase (CRTH) Parameter MA (mm) Heparinase is included in the subject device	RapidTEG™ MA is the point at which clot strength reaches its maximum and reflects the end result of minimal platelet-fibrin interaction via the GPIIb/IIIa receptors. Due to faster coagulation activation, clot strength is measured faster than Citrated: Kaolin (K) activated samples. Same results as CK maximum amplitude (CK-MA). The MA provides information about the contribution of platelets/fibrin to the overall strength of the clot.	RapidTEG MA is the point of maximal amplitude of the TEG tracing, measured in mm, and reflects the maximum clot strength. The strength of the clot is primarily a result of platelet–fibrin interactions via the GPIIb/IIIa receptors. *Clinical Value:* The MA provides information of platelets and fibrinogen contribution to the overall clot strength. A decreased MA is indicative of low clot strength, which could be due to decreased platelet or decreased fibrinogen contribution; whereas an increased MA is indicative of high clot strength, which could be due to increased platelet or fibrinogen contribution.
Clinical Value of Citrated: Functional Fibrinogen with Heparinase (CFFH) Parameter MA (mm)	The maximum amplitude of CFF provides the functional fibrinogen contribution to the clot strength. Provides the overall contribution of functional fibrinogen to clot	The Functional Fibrinogen reagent inhibits platelet aggregation via the GPIIb/IIIa receptor, excluding its contribution to clot strength (MA), and thereby primarily measures the

Heparinase is included in the subject device	strength. In conjunction with CRT-MA, this assay enables an assessment of the relative contributions of functional fibrinogen and platelets to clot strength. Results may be valuable for guiding fibrinogen supplementation or platelet transfusion.	functional fibrinogen contribution to clot strength. *Clinical Value:* CFFH - MA provides the fibrinogen contribution to clot strength by exclusion of platelet aggregation. In conjunction with CRTH-MA, this assay enables the contributions of fibrin and platelets to clot strength to be determined.

6. Non-Clinical and/or Clinical Tests Summary & Conclusions

Non-Clinical Performance Testing

A. Reference Ranges

Expected values for test results are within the Reference Ranges for a reference population that were established according to CLSI EP28-A3c. Citrated whole blood from normal donors (representative of normal population distributions – age, gender, race) with no known coagulopathies and not taking any drugs that would potentially affect patient hemostasis was used. Non-parametric method for analysis was used to determine the reference range for each assay parameter. The following tables contain the reference range data for each reagent and parameter.

CK Reference Ranges

Citrated Blood Parameter	N	Range
R (min)	157	4.6-9.1
MA (mm)	151	52-69

CKH Reference Ranges

Citrated Blood Parameter	N	Range
R (min)	155	4.3-8.3
LY30 (%)	148	0-3.2

CRTH Reference Ranges

Citrated Blood Parameter	N	Range
MA (mm)	162	53-69

CFFH Reference Ranges

Citrated Blood Parameter	N	Range
MA (mm)	162	15-34

B. Analytical Precision (Repeatability and Reproducibility)

Several studies were performed to support the Precision (Repeatability and Reproducibility) of the Citrated: K, KH, RTH, FFH assay cartridge. Studies performed with Cartridge Reagent QC Level 1 and Level 2 materials included a multi-site reproducibility study and a single-site repeatability study in accordance with the CLSI-EP05 A3 guideline, and a within lab lot to lot precision study. Two additional studies were performed with normal whole blood samples and contrived hypocoagulable, hypercoagulable and hyperfibrinolytic blood samples.

Citrated: K, KH, RTH, FFH Cartridge Reagent QC Precision

Several test protocols were executed as part of Citrated: K, KH, RTH, FFH assay cartridge (PN 07-604-US) performance verification on the TEG® 6s Hemostasis System with Cartridge Reagent QC Level 1 and Level 2 materials:

Each data set includes evaluation of different sources of variation, these were combined to generate an assessment of the Citrated: K, KH, RTH, FFH assay cartridge combined QC precision for a worst case estimate of total precision.

Cartridge Reagent QC Precision Studies – Overview

Study	Multi-site	Cartridge Lot to Lot	Operator to Operator	Repeatability
	TR-DIS-102653-C	TR-DIS-102583-C	TR-DIS-102697-C	TR-DIS-102697-C
Instrument	**3 in combination per site**	6 confounded with rep	1 instrument/control l	1 instrument/control
Operator		**2 operators**	**2 operators**	1 operator
Day	**5 days**	**10 days**	**10 days**	**20 days**
Cartridge Lot	1 lot	**3 lots**	1 lot	1 lot
QC Lot	1 lot	**2 lots**	1 lot	1 lot
Run	1 run/day	1 run/day	**2 runs**	**2 runs**
Rep	**5 reps/control/site**	1 rep	**2 reps/control**	**2 reps/control**
Total N	**75**	**120**	**80**	**80**
Study Design	**Nested**	**Crossed**	**Nested**	**Nested**

Results of the QC precision studies demonstrate that Citrated: K, KH, RTH, FFH assay cartridge achieves repeatability, within laboratory, reproducibility and total precision requirements on all reported parameters for Cartridge Reagent QC Level 1 and Cartridge Reagent QC Level 2.

CARTRIDGE REAGENT QC PRECISION – SUMMARY OF RESULTS

Sample	Assay-Parameter	N	Mean	Repeatability		Between Run		Between Day		Between Cartridge Lot		Between QC Lot		Between Site *Instrument/Operator*		Total		Pass/ Fail
				SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	
Cartridge Reagent QC Level 1 (07-664)	CK-R (min)	316	6.16	0.54	8.9%	0.00	0.0%	0.27	4.4%	0.02	0.4%	0.12	2.0%	0.39	6.3%	0.73	11.9%	Pass
	CKH-R (min)	316	4.62	0.41	8.5%	0.09	2.0%	0.14	3.1%	0.12	2.5%	0.25	5.2%	0.26	5.7%	0.58	12.3%	Pass
	CK-MA (mm)	316	66.85	1.57	2.4%	0.00	0.0%	0.48	0.7%	0.00	0.0%	1.37	2.1%	0.56	0.8%	2.21	3.3%	Pass
	CRTH-MA (mm)	316	59.36	1.81	3.0%	0.00	0.0%	0.95	1.6%	0.00	0.0%	0.00	0.0%	1.76	2.9%	2.70	4.5%	Pass
	CFFH-MA (mm)	316	63.80	1.35	2.1%	0.00	0.0%	1.05	1.7%	0.61	1.0%	0.00	0.0%	2.11	3.3%	2.78	4.4%	Pass
	CKH LY30 (%)	196*	0.00	0.00	n/a	0.00	n/a	0.00	n/a	0.00	n/a	0.00	n/a	0.00	n/a	0.00	n/a	Pass
Cartridge Reagent QC Level 2 (07-665)	CK-R (min)	316	1.18	0.09	7.0%	0.05	3.6%	0.04	2.8%	0.01	0.7%	0.06	5.0%	0.03	2.7%	0.12	10.1%	Pass
	CKH-R (min)	316	1.18	0.09	7.2%	0.02	1.5%	0.03	2.4%	0.00	0.0%	0.07	5.7%	0.03	2.8%	0.12	10.0%	Pass
	CK-MA (mm)	313	27.64	1.51	5.4%	1.01	3.7%	0.84	3.1%	0.23	0.8%	0.72	2.6%	0.51	1.8%	2.20	8.0%	Pass
	CRTH-MA (mm)	316	29.03	1.52	5.2%	0.76	2.7%	0.89	3.2%	0.30	1.0%	0.83	2.8%	0.81	2.7%	2.26	7.8%	Pass
	CFFH-MA (mm)	316	28.69	1.26	4.5%	0.95	3.4%	0.91	3.3%	0.13	0.5%	0.95	3.3%	0.68	2.3%	2.17	7.7%	Pass
	CKH-Ly30 (%)	316	92.42	0.46	0.5%	0.40	0.4%	0.12	0.1%	0.04	0.0%	0.10	0.1%	0.00	0.0%	0.63	0.7%	Pass

Citrated: K, KH, RTH, FFH Cartridge Whole Blood Repeatability

Two studies were conducted for Whole Blood Repeatability on the Citrated: K, KH, RTH, FFH assay cartridge. Testing was conducted with normal donor whole blood and contrived hyper-coagulable, hypo-coagulable, and hyper-fibrinolytic whole blood samples. The following table summarizes the sample types evaluated:

WHOLE BLOOD PRECISION STUDIES - SAMPLE TYPES

Sample Type #	Hemostatic State	Assay & Parameter Applicability with expected result impact [increase (↑) or decrease (↓) from un-spiked "Neat" sample]						Method or Additive for Contriving*
		CK R	CKH R	CK MA	CRTH MA	CFFH MA	CKH LY30	
1	Normal	x	x	x	x	x	x	None
2	Contrived Hypo-coagulable	x↑	x↑	x↓	x↓			Abciximab and Dabigatran
3	Contrived Hypo-coagulable					x↓		Dilution and /or Fibrinogen depletion
4	Contrived Hyper-coagulable			x↑	x↑			Platelet Rich Plasma and Fibrinogen
5	Contrived Hyper-coagulable					x↑		Fibrinogen

6	Contrived Hyper-fibrinolytic						**x↑**	tPA
7	Contrived Hyper-coagulable	**x↓**	**x↓**					Tissue factor

Whole Blood precision testing was conducted at a one (1) location, using two (2) operators, three (3) cartridge lots. For the normal whole blood samples, each operator performed 2 replicates/sample/cartridge lot on each of 2 analyzers for a total N= 12 per operator. For the contrived samples, each operator performed 1 replicate/sample simultaneously on 4 different analyzers/cartridge lot for a total N =12 per operator. Each contrived sample was prepared just prior to execution of testing.

Data collected for each sample was analyzed separately through an ANOVA for precision. Results are summarized in the tables below:

WHOLE BLOOD PRECISION REPEATABILITY SUMMARY – NORMAL SAMPLE

Sample	**Assay Parameter**	**N**	**Mean**	**Repeatability**		**Between Operator**		**Between Lot**		**Between Device/Day**		**Within Laboratory** *(= Total Precision)*		**Pass /Fail**
				SD	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	
S1 Normal Donor Whole Blood	CK R (min)	24	7.50	0.44	5.9%	0.00	0.0%	0.65	8.7%	0.28	3.8%	0.83	11.2%	Pass
	CKH R (min)	24	7.60	0.75	10.0%	0.00	0.0%	0.00	0.0%	0.14	1.8%	0.77	10.1%	Pass
	CK MA (mm)	24	54.80	0.96	1.7%	0.32	0.6%	0.54	1.0%	0.25	0.5%	1.17	2.1%	Pass
	CRTH MA (mm)	24	17.00	0.27	1.6%	0.46	2.7%	0.09	0.6%	0.60	3.5%	0.81	4.8%	Pass
	CFFH MA (mm)	24	57.00	1.43	2.5%	0.65	1.1%	0.20	0.4%	0.00	0.0%	1.58	2.8%	Pass
	CKH LY30 (%)	24	0.30	0.13	51.0%	0.00	0.0%	0.10	36.5%	0.08	32.1%	0.18	70.4%	Pass

WHOLE BLOOD PRECISION REPEATABILITY SUMMARY – CONTRIVED ABNORMAL SAMPLES

Sample	**Assay Parameter**	**N**	**Mean**	**Repeatability***		**Between Operator**		**Between Lot**		**Within Laboratory** *(= Total Precision)*		**Pass /Fail**
				SD	**CV**	**SD**	**CV**	**SD**	**CV**	**SD**	**CV**	
S2 Contrived Hypo-Coagulable (R↑, MA↓)	CK R (min)	24	13.29	1.47	11.1%	0.00	0.0%	0.00	0.0%	1.47	11.1%	Pass
	CKH R (min)	24	13.09	1.52	11.6%	0.61	4.6%	0.39	3.0%	1.68	12.8%	Pass
	CK MA (mm)	24	52.78	1.04	2.0%	0.00	0.0%	0.89	1.7%	1.37	2.6%	Pass
	CRTH MA (mm)	24	58.55	0.51	0.9%	0.00	0.0%	0.35	0.69%	0.62	1.1%	Pass
	CFFH MA (mm)	24	18.02	0.17	1.0%	0.03	0.2%	0.12	0.76%	0.21	1.2%	Pass
	CKH LY30 (%)	24	1.18	0.19	16.1%	0.00	0.0%	0.00	0.0%	0.19	16.1%	Pass
S3 Contrived	CK R (min)	24	4.91	0.31	6.3%	0.03	0.7%	0.12	2.4%	0.33	6.8%	Pass

Sample	Assay Parameter	N	Mean	Repeatability*		Between Operator		Between Lot		Within Laboratory *(= Total Precision)*		Pass /Fail
				SD	CV	SD	CV	SD	CV	SD	CV	
Hypo-Coagulable (MA↓)	CKH R (min)	24	4.85	0.20	4.2%	0.00	0.0%	0.11	2.4%	0.23	4.8%	Pass
	CK MA (mm)	24	44.71	0.69	1.6%	0.49	1.1%	0.39	0.9%	0.94	2.1%	Pass
	CRTH MA (mm)	24	43.52	1.16	2.7%	0.24	0.6%	0.00	0.0%	1.19	2.7%	Pass
	CFFH MA (mm)	24	10.08	0.83	8.2%	0.24	2.4%	0.33	3.3%	0.92	9.2%	Pass
	CKH LY30 (%)	*Data not collected*										
S4 Contrived Hyper-coagulable (MA↑)	CK R (min)	23	5.47	0.61	10.7%	0.37	6.5%	0.05	0.8%	0.71	12.5%	Pass
	CKH R (min)	23	5.91	0.72	12.2%	0.00	0.0%	0.46	7.8%	0.85	14.5%	Pass
	CK MA (mm)	23	70.96	0.35	0.5%	0.27	0.4%	0.27	0.4%	0.51	0.7%	Pass
	CRTH MA (mm)	24	71.59	0.39	0.5%	0.00	0.0%	0.00	0.0%	0.39	0.5%	Pass
	CFFH MA (mm)	24	51.38	0.92	1.8%	0.78	1.5%	2.81	5.5%	3.06	6.0%	Pass
	CKH LY30 (%)	*Data not collected*										
S5 Contrived Hyper-coagulable (MA↑)	CK R (min)	24	6.60	0.51	7.7%	0.10	1.5%	0.24	3.6%	0.57	8.6%	Pass
	CKH R (min)	24	6.28	0.66	10.6%	0.00	0.0%	0.24	3.8%	0.71	11.2%	Pass
	CK MA (mm)	24	63.85	0.75	1.2%	0.00	0.0%	0.19	0.3%	0.77	1.2%	Pass
	CRTH MA (mm)	24	66.59	0.26	0.4%	0.00	0.0%	0.13	0.2%	0.29	0.4%	Pass
	CFFH MA (mm)	24	32.92	0.66	2.0%	0.00	0.0%	0.53	1.6%	0.85	2.6%	Pass
	CKH LY30 (%)	24	0.45	0.44	97.1%	0.00	0.0%	0.14	31.0%	0.46	101.9%	Pass
S6 Contrived Hyper-fibrinolytic (LY30↑)	CK R (min)	24	6.38	0.45	7.1%	0.00	0.0%	0.51	8.0%	0.68	10.7%	Pass
	CKH R (min)	24	6.53	0.54	8.3%	0.00	0.0%	0.00	0.0%	0.54	8.3%	Pass
	CK MA (mm)	24	58.69	0.96	1.6%	0.00	0.0%	0.10	0.2%	0.96	1.6%	Pass
	CRTH MA (mm)	24	61.56	0.68	1.1%	0.38	0.6%	0.00	0.0%	0.78	1.3%	Pass
	CFFH MA (mm)	24	21.70	1.01	4.6%	0.28	1.3%	1.25	5.7%	1.63	7.5%	Pass
	CKH LY30 (%)	23	15.87	1.59	9.7%	0.00	0.0%	0.00	0.0%	1.59	9.7%	Pass
S7 Contrived Hyper-	CK R (min)	24	4.41	0.17	3.8%	0.00	0.0%	0.13	2.9%	0.21	4.8%	Pass
	CKH R (min)	24	4.31	0.19	4.3%	0.00	0.0%	0.08	1.9%	0.20	4.7%	Pass

Sample	Assay Parameter	N	Mean	Repeatability*		Between Operator		Between Lot		Within Laboratory *(= Total Precision)*		Pass /Fail
				SD	CV	SD	CV	SD	CV	SD	CV	
Coagulable (R↓)	CK MA (mm)	24	64.38	0.44	0.7%	0.11	0.2%	0.28	0.4%	0.54	0.8%	Pass
	CRTH MA (mm)	24	65.65	0.40	0.6%	0.16	0.2%	0.00	0.0%	0.43	0.6%	Pass
	CFFH MA (mm)	24	25.18	0.43	1.7%	0.17	0.7%	0.52	2.1%	0.69	2.7%	Pass
	CKH LY30 (%)	24	0.67	0.15	23.1%	0.03	4.2%	0.13	20.0%	0.21	30.8%	Pass

** Repeatability for contrived abnormal samples includes analyzer variation*

Summarized Precision for each channel is as follows:

CK Precision

The precision of the Kaolin test was evaluated according to CLSI EP5-A3. Precision testing was performed with Cartridge Reagent QC Level 1 and Level 2, normal and contrived hyper-coagulable, hypo-coagulable, and hyper-fibrinolytic whole blood samples using multiple donors, cartridge lots, operators and analyzers. Results included Coefficient of Variance (CV) values for all precision tests. The CV of the test results for the Kaolin assay was less than 15% for the R parameter and less than 10% for the MA parameter.

CKH Precision

The precision of the Kaolin with heparinase test was evaluated according to CLSI EP5-A3. Precision testing was performed with Cartridge Reagent QC Level 1 and Level 2, normal and contrived hyper-coagulable, hypo-coagulable, and hyper-fibrinolytic whole blood samples using multiple donors, cartridge lots, operators and analyzers. Results included Coefficient of Variance (CV) values for all precision tests. The CV of the test results for the Kaolin with heparinase assay was less than 15% for the R parameter.

CRTH Precision

The precision of the RapidTEG with heparinase test was evaluated according to CLSI EP5-A3. Precision testing was performed with Cartridge Reagent QC Level 1 and Level 2, normal and contrived hyper-coagulable, hypo-coagulable, and hyper-fibrinolytic whole blood samples using multiple donors, cartridge lots, operators and analyzers. Results included Coefficient of Variance (CV) values for all precision tests. The CV of the test results for the RapidTEG with heparinase assay was less than 10% for the MA parameter.

CFFH Precision

The precision of the Functional Fibrinogen test with heparinase was evaluated according to CLSI EP5-A3. Precision testing was performed with Cartridge Reagent QC Level 1 and Level 2, normal and contrived hyper-coagulable, hypo-coagulable, and hyper-fibrinolytic whole blood samples using multiple donors, cartridge lots, operators and analyzers. Results included Coefficient of Variance (CV) values for all precision tests. The CV of the test results for the Functional Fibrinogen with heparinase assay was less than 15% for the MA parameter.

C. Interference

Testing for interfering factors was conducted according to CLSI EP07-A3 using whole blood from normal donor, contrived hyperfibrinolytic, and contrived hypocoagulable specimens. Potential interferents and levels tested are indicated in the following table:

Interfering Factors (levels)	Specimen Type	Highest Concentration with No Interference					
		CK - R	CK - MA	CKH - R	CKH - LY30	CRTH - MA	CFFH - MA
No Discard Tube	Normal	NI	NI	NI	NI	NI	NI
	Hypocoagulable	NI	NI	NI	NI	NI	NI
	Hyperfibrinolytic	NI	NI	NI	Yes	NI	NI
Hemolysis (0, 50, 100, 200, 400 mg/dL)	Normal	400	400	400	200	400	400
	Hypocoagulable	400	400	400	400	400	400
	Hyperfibrinolytic	400	400	200	0	100	400
Short Draw (% fill in a 3.2% sodium citrate Vacutainer® tube: 100, 90, 80, 70 and 60%)	Normal	60% Fill	60% Fill	60% Fill	60% Fill	70% Fill	60% Fill
	Hypocoagulable	60% Fill	60% Fill	70% Fill	60% Fill	60% Fill	60% Fill
	Hyperfibrinolytic	60% Fill	60% Fill	60% Fill	70% Fill	60% Fill	60% Fill
Dilution (0%, 20%, 30%, 40%, 50%)	Normal	50%	20%	50%	50%	20%	40%
	Hypocoagulable	50%	0%	50%	50%	0%	40%
	Hyperfibrinolytic	50%	0%	50%	0%	0%	20%
Dabigatran (0, 45, 90, 135, 180 ng/mL)	Normal	0	180	0	90	180	180
	Hypocoagulable	NT	NT	NT	NT	NT	NT
	Hyperfibrinolytic	0	90	0	0	180	180
Rivaroxaban (0, 50, 100, 200, 400 ng/mL)	Normal	50	400	50	400	400	400
	Hypocoagulable	NT	NT	NT	NT	NT	NT
	Hyperfibrinolytic	50	200	50	400	400	400
Aspirin	Normal	6.5	6.5	6.5	6.5	6.5	6.5

Interfering Factors (levels)	Specimen Type	Highest Concentration with No Interference					
		CK - R	CK - MA	CKH - R	CKH - LY30	CRTH - MA	CFFH - MA
(0, 6.5 mg/dL)	Hypocoagulable	NT	NT	NT	NT	NT	NT
	Hyperfibrinolytic	6.5	6.5	6.5	0	6.5	6.5
Ticagrelor (0, 1.8 ug/mL)	Normal	1.8	1.8	1.8	1.8	1.8	1.8
	Hypocoagulable	NT	NT	NT	NT	NT	NT
	Hyperfibrinolytic	1.8	1.8	1.8	1.8	1.8	1.8
Alcohol (0, 40, 80, 160, 320 mg/dL)	Normal	320	320	320	320	320	320
	Hypocoagulable	320	320	320	320	320	320
	Hyperfibrinolytic	320	320	320	320	320	320
Lipemia (0, 150, 300, 450, 600 mg/dL)	Normal	600	600	600	600	600	600
	Hypocoagulable	600	600	600	600	600	600
	Hyperfibrinolytic	600	600	600	600	600	600
TXA (0, 100, 200 ug/mL)	Normal	200	200	200	200	200	200
	Hypocoagulable	200	200	200	200	200	200
	Hyperfibrinolytic	NT	NT	NT	NT	NT	NT
EACA (0, 300, 600 ug/mL)	Normal	600	600	600	600	600	600
	Hypocoagulable	600	600	600	600	600	600
	Hyperfibrinolytic	NT	NT	NT	NT	NT	NT
Mycophenolic Acid (21, 42 ug/mL) (5, 10, 21, 42 (ug/mL))	Normal	42	42	42	42	42	42
	Hypocoagulable	42	42	42	42	42	42
	Hyperfibrinolytic	42	42	42	42	42	42
Tacrolimus (70, 144 ng/mL)	Normal	144	144	144	144	144	144
	Hypocoagulable	144	144	144	144	144	144
	Hyperfibrinolytic	144	144	144	144	144	144
Prednisone (45, 99 ng/mL)	Normal	99	99	99	99	99	99
	Hypocoagulable	99	99	99	99	99	99
	Hyperfibrinolytic	99	99	99	99	99	99
Rifaximin (20, 40.5 ng/mL) (5, 10, 20, 40.5 ng/mL)	Normal	40.5	40.5	40.5	40.5	40.5	40.5
	Hypocoagulable	40.5	40.5	40.5	40.5	40.5	40.5
	Hyperfibrinolytic	40.5	40.5	40.5	40.5	40.5	40.5
Lactulose (6, 12 ug/mL)	Normal	12	12	12	12	12	12
	Hypocoagulable	12	12	12	12	12	12
	Hyperfibrinolytic	12	12	12	12	12	12

Legend:
NI - No Interference
NT - Not Tested

D. Measurement Interpretation Guidance

The measurement interpretation guidance table that follows is based on in vitro studies that examined individual values of assays and parameters with respect to their reference ranges. Only one or a few variables influencing TEG results were systematically varied while other variables were kept constant.

The measurement interpretation guidance table is not intended to be comprehensive of all variables that could influence test results, but addresses key variables based on literature review and clinical experience. As with any hemostasis test, TEG® 6s test results should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests.

Assay	Parameter (Units)	Ref Range (RR)	Parameter Readout	Hemostatic Significance of Individual Parameter	Interpretation of Parameter Readout for Consideration
CK	R (min)	4.6 – 9.1	CK-R > RR	Hypocoagulable	↓Coagulation factor activity and/or presence of heparin at sufficiently high concentrations
			CK-R < RR	Hypercoagulable	
	MA (mm)	52 – 69	CK-MA < RR	Hypocoagulable	↓Fibrinogen or ↓Platelet Contribution
			CK-MA > RR	Hypercoagulable	↑Fibrinogen or ↑Platelet Contribution
CKH	R (min)	4.3 – 8.3	CK-R > CKH-R	Heparin Effect	Indicative of heparin effect
			CKH-R > RR	Hypocoagulable	↓Coagulation factor activity and/ or presence of non-heparin anticoagulants
	LY30 (%)	0 – 3.2	CKH-LY30 > RR	Hypocoagulable	Hyperfibrinolysis
CRTH	MA (mm)	53 – 69	CRTH-MA < RR	Hypocoagulable	↓Fibrinogen or ↓Platelet Contribution
			CRTH-MA > RR	Hypercoagulable	↑Fibrinogen or ↑Platelet Contribution
CFFH	MA (mm)	15 – 34	CFFH-MA < RR	Hypocoagulable	↓Fibrinogen
			CFFH-MA > RR	Hypercoagulable	↑Fibrinogen

Citrated Kaolin (CK)

The Citrated Kaolin TEG assay uses kaolin for activation of coagulation. Kaolin activation has traditionally been described as intrinsic pathway activation.

CK - R

Kaolin R is the time in minutes elapsing between sample activation and the point in time where clotting provides enough resistance to produce a 2 mm amplitude reading on the TEG® 6s analyzer tracing. The CK - R parameter represents the initiation phase of coagulation triggered by enzymatic clotting factors and culminating with the initial fibrin formation. A prolonged R value is indicative of slow clot formation, and a shortened R value is indicative of fast clot formation.

Clinical Value: A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies, heparin, or other anticoagulants.

CK-MA

The maximal strength of the clot when activated with kaolin. This represents the combination of the contribution of fibrinogen and platelets to clot strength.

Clinical Value: The MA provides information of platelets and fibrinogen to the overall clot strength without excluding the influence of heparin. A decreased MA is indicative of low clot strength, which could be due to decreased platelet contribution or decreased fibrinogen; whereas, an increased MA is indicative of high clot strength, which could be due to increased platelet or fibrinogen contribution.

Citrated Kaolin with Heparinase (CKH)

CKH - R

The reaction time between initiation of the clot (via kaolin) and the point where the tracing reaches 2 mm of amplitude, with heparinase being used to neutralize the effect of heparin.

Clinical Value: A prolonged R value is indicative of slow clot formation, due to coagulation factor deficiencies or non-heparin anticoagulant. A shortening of the CKH-R compared to the CK-R indicates effect of heparin in the blood sample.

CKH - LY30

Clot lysis, in a sample with heparinase to neutralize effects of heparin, expressed as a percent reduction in clot strength 30 minutes after the MA is reached.

Clinical Value: LY30 provides information about fibrinolytic activity.

Citrated RapidTEG™ with Heparinase (CRTH)

The RapidTEG assay incorporates both tissue factor and kaolin, which simultaneously activate the extrinsic and intrinsic coagulation pathways. The assay accelerates coagulation compared to the conventional Kaolin test. Heparinase is added to neutralize heparin in the sample.

CRTH - MA

RapidTEG MA is the point of maximal amplitude of the TEG tracing, measured in mm, and reflects the maximum clot strength. The strength of the clot is primarily a result of platelet–fibrin interactions via the GPIIb/IIIa receptors.

Clinical Value: The MA provides information of platelets and fibrinogen to the overall clot strength. A decreased MA is indicative of low clot strength, which could be due to decreased platelet contribution or decreased fibrinogen; whereas, an increased MA is indicative of high clot strength, which could be due to increased platelet or fibrinogen contribution.

Citrated Functional Fibrinogen with Heparinase (CFFH)

The Citrated Functional Fibrinogen assay activates the extrinsic pathway using tissue factor and inhibits platelet aggregation using a platelet inhibitor that binds to GPIIb/IIIa receptors. Heparinase is added to neutralize heparin in the sample.

CFFH - MA

The Functional Fibrinogen reagent inhibits platelet aggregation via the GPIIb/IIIa receptor, excluding its contribution to clot strength (MA), and thereby primarily measures the functional fibrinogen contribution to clot strength.

Clinical Value: CFFH - MA provides the fibrinogen contribution to clot strength by exclusion of platelet aggregation. In conjunction with CRTH-MA, this assay enables the contributions of fibrin and platelets to clot strength to be determined.

E. CK Sensitivity and Specificity

Two studies were performed to define the sensitivity and specificity for the CK channel. Blood samples were collected from four normal donors and from four donors (four unique donors for each condition) and contrived to simulate hypocoagulable, hypercoagulable and hyperfibrinolytic conditions. Final heparin concentration in tested samples were 0, 0.1, 0.15 and 0.2 IU.

For Normal donors, a 95% specificity in samples without heparin and a 95% sensitivity for detection of heparin at 0.2 IU/ml was calculated using blood samples from four donors. All contrived hypo-coagulable, hyper-coagulable and hyper-fibrinolytic samples without heparin showed 100% specificity and all samples spiked at 0.2 IU/ml showed 100% sensitivity for the detection of heparin. A summary of cumulative results is shown in the table below.

Cumulative Results (total N=20, 4 Donors/condition evaluated)			
Sample Condition	**Heparin Concentration (IU/mL)**	**Sensitivity %**	**Specificity %**
Normal	0	N/A	95 %
	0.1	95 %	N/A
	0.15	100 %	N/A
	0.2	95 %	N/A
Contrived Hypo-coagulable	0	N/A	100 %
	0.1	100 %	N/A
	0.15	100 %	N/A
	0.2	100 %	N/A
Contrived Hyper-coagulable	0	N/A	100 %
	0.1	100 %	N/A
	0.15	100 %	N/A
	0.2	100 %	N/A
Contrived Hyper-fibrinolytic	0	N/A	100 %
	0.1	95 %	N/A
	0.15	100 %	N/A
	0.2	**100 %**	N/A

F. Assay Measuring Range

The Assay Measuring Range (AMR) study was performed to establish the analytical measurement ranges for MA (CRTH and CFFH channels) and LY30 (CKH channel) for the Citrated: K, KH, RTH, FFH assay cartridge and to demonstrate verification of required %CV for each parameter. The high and low boundaries of AMR values for MA and LY30 obtained from the study are as follows:

Parameter	Lower AMR	Calculated CV (%)	Upper AMR	Calculated CV (%)
CRTH-MA	20	2.8	78	0.9
CFFH-MA	6	8.7	61	1.4
CKH-LY30	0	0	30	5.1

As there are no changes in assay composition and formulation of CK and CKH channels in the Citrated: K, KH, RTH, FFH assay cartridge compared to existing channels in the Citrated Multichannel Cartridge (CM), previously established AMR values for CK-R (lower AMR of 0.4 and upper AMR of 17), CK-MA (lower AMR of 40 and upper AMR of 70) and CKH-R (lower AMR of 0.3 and upper AMR of 17) parameters, will also be used for the Citrated: K, KH, RTH, FFH assay cartridge.

The Assay Measuring Range values available from the TEG 6s with the Citrated Multichannel Cartridge (K150041, 07-601-US) are being retained for the Citrated: K, KH, RTH, FFH assay cartridge.

Parameter	Lower AMR	Upper AMR
CK-R	0.4	17
CK-MA	40	75
CKH-R	0.3	17

G. Heparin Neutralization Requirement Verification

The use of heparinase neutralizes the effect of heparin in the blood sample. Tests were performed using Unfractionated Heparin (UFH) and Low Molecular Weight Heparin (LMWH) spiked samples and un-spiked samples. All tests reported R parameter values within the normal range, confirming the neutralization effectiveness of the assay. Functional performance of the cartridges were verified against heparin neutralization requirements. A total of 200 cartridges were tested across four donors, and 10 replicates.

The mean result per test specimen condition fell within the respective normal reference range for CRTH-MA, CFFH-MA, CKH-R, and CKH-LY30 for all donors. The study acceptance criteria were met and has verified the defined heparin neutralization performance requirements:

Requirement Description	**Acceptance Criteria Pass/Fail**
The CKH, CRTH, and CFFH assays shall be able to neutralize up to 5.0 IU/mL (+/- 0.1IU/mL) of heparin. (CTQ)	Pass
The CKH, CRTH, and CFFH assays shall be able to neutralize up to 0.013 mg/mL (+/- 0.001 mg/mL) of LMWH. (CTQ)	Pass

The tolerance interval (95% confidence for 90% of the population) calculated for CFFH-MA, and CRTH-MA for all specimen types fell within the respective normal reference range. The study acceptance criteria were met and has verified the following heparin neutralization performance requirements:

Requirement Description	**Acceptance Criteria Pass/Fail**
Blood treated with 5.0 IU/ml (+/- 0.1IU/mL) of heparin, measured CFFH MA, shall remain within the normal reference range, 90% of the time. (CTQ)	Pass

Blood treated with 5.0 IU/ml (+/- 0.1IU/mL), measured CRTH MA, shall remain within the normal reference range, 90% of the time. (CTQ)	Pass

For all 0.008 mg/mL LMWH contrived samples, the CK-R value was greater than the CKH-R value. The study acceptance criteria were met and has verified the following heparin neutralization performance requirement for the LMWH sample condition:

Requirement Description	Acceptance Criteria Pass/Fail
CK R shall be greater than CKH R when at least 0.2 IU/mL of heparin or at least 0.008 mg/mL LMWH is present in the blood sample. (CTQ)	Pass

Clinical Performance Testing

Clinical Performance - Method Comparison

A Method Comparison study was conducted with patient samples collected at eight clinical trial sites, following CLSI EP09-A3 guidelines. The subjects enrolled were patients undergoing liver transplantation, cardiovascular surgery, or cardiology procedures. Blood samples were drawn before, during, and after the procedures and were analyzed using TEG® 6s analyzers with the Citrated: K, KH, RTH, FFH (Global Hemostasis - HN) cartridge, as well as the TEG 6s with the associated Cartridge (Citrated Multichannel Cartridge) and Clauss Fibrinogen as the comparators. Summary statistics are presented below.

Assay Parameter	N of Samples	Intercept [95% CI)	Slope [95% CI]	Pearson Corr. [95% CI]	Spearman Corr. [95% CI]
CK - R	617	-0.45 [-0.769; -0.125]	1.08 [1.041; 1.126]	0.90 [0.878; 0.910]	--
CK - MA	539	-3.43 [-5.127; -1.731]	1.05 [1.022; 1.082]	0.95 [0.939; 0.956]	--
CKH - R	829	-0.17 [-0.538; 0.193]	1.01 [0.960; 1.055]	0.82 [0.800; 0.844]	--
CKH - LY30	828	-0.01 [-0.095; 0.071]	1.00 [0.988; 1.010]	0.99 [0.985; 0.989]	--
CRTH - MA	870	-5.54 [-6.626; -4.459]	1.11 [1.094; 1.133]	0.97 [0.962; 0.971]	--
CFFH - MA *	883	-78.71 [-98.9; -58.53]	1.32 [1.25; 1.40]	--	0.79 [0.757; 0.814]

*Clauss Fibrinogen comparator

Three assessment types were assigned due to the differing comparisons that were to be made for the parameters of the assays in the Citrated: K, KH, RTH, FFH assay cartridge.

Assessment Type	Citrated: K, KH, RTH, FFH Parameters	Predicate/Comparative Device Description
1	CK-R CK-MA CKH-R CKH-LY30	The parameters in the predicate are identical with the Citrated: K, KH, RTH, FFH assay cartridge
2	CRTH-MA	The CKH-MA on the predicate device is an equivalent channel
3	CFFH-MA	Clauss fibrinogen plasma concentration allows comparison of contribution of fibrinogen to clot formation

The assessment of equivalency between the CK, CKH, CRTH, and CFFH channels on the cartridge with its comparators was primarily based on the assessment of the bias at the medical decision points relative to the acceptable limits of the bias and the analysis of the relationship between the device parameters and their respective comparators.

For each parameter of Type 1 and Type 2, the predicted bias estimates at the lower and upper limits of the normal reference range (NRR) were within the acceptable bias limits. The entire confidence intervals for the predicted biases of all parameters were contained within the acceptable bias limits at the lower and upper limits of the NRR for all parameters, passing and exceeding pre-established bias acceptance criteria at the medical decision points and indicating excellent agreement. In summary, for all parameters, the assessment of the predicted bias and its 95% confidence interval relative to the pre-established bias acceptance criteria at the medical decision points suggested equivalence according to the CLSI EP09-A3.

The linear regression slope estimates, for all primary between-device comparisons of Type 1 and 2 parameters, were close to 1.0 with their respective 95% confidence intervals containing 1.0 with Pearson correlation coefficients greater than 0.82 in all cases. Slope estimates for the primary parameters (CKH-R, CKH-LY30, CRTH-MA) ranged from 1.00 to 1.11. The origin was contained in the 95% confidence interval of the intercept for each of the Type 1 and Type 2 parameters.

Type 3 parameters were defined as parameters that measure a different physical property,

i.e., the maximum amplitude on the CFFH channel (CFFH-MA) than the comparator, the Clauss fibrinogen plasma concentration. However, the two parameters were expected to convey similar information, i.e., the contribution of fibrinogen to clot formation. There was no expectation of a perfect linear relationship between the two parameters as viscoelastic testing measures the functionality of large parts of the coagulation cascade and not an individual analyte, i.e., fibrinogen. Regression analysis for the Type 3 parameter, CFFH-MA on the Citrated: K, KH, RTH, FFH assay cartridge, with its comparator, Clauss fibrinogen plasma concentration, yielded a Spearman correlation coefficient of 0.79 [0.757; 0.814] .

Secondary within-device comparison analysis confirmed that the entire confidence intervals for the predicted biases of all parameters were contained within the acceptable bias limits at the lower and upper limits of the NRR for all parameters, passing and exceeding pre-established bias acceptance criteria at the medical decision points and indicating excellent reproducibility.

Repeatability for all parameters (i.e., Replicate 2 vs. Replicate 1, measured with two Citrated: K, KH, RTH, FFH cartridges) resulted in Pearson linear correlation coefficients that were above 0.88 for all parameters. Another important outcome of the study was that the new heparinase-containing parameters CRTH-MA and CFFH-MA yielded over 90% of samples contributing to the final data set at each of the three time points, irrespective of whether heparin was typically present at theses time points or not and similar to the percentage of samples contributing in the CKH-channels. This high number of contributing samples suggests that the incidence of heparin-induced data quality issues was reduced in these channels versus non-heparinase containing channels, suggesting the feasibility of coagulation assessment under conditions of the presence of heparin and/or its reversal agents.

Method comparison data supports the equivalency of the Citrated: K, KH, RTH, FFH assay cartridge parameters and their respective comparators. Within-device replicability was excellent in each case. The data suggests that the feasibility of obtaining diagnostic information with the novel CRTH-MA and CFFH-MA parameters enables the measurement of these parameters in the presence of heparin and/or its reversal agents.

7. Electrical safety and electromagnetic compatibility (EMC)

Electrical safety and EMC testing were conducted on the TEG® 6s hemostasis analyzer. The system complies with the IEC 61010-1, IEC 61010-2-010, IEC 61010-2-101, standards for safety and the IEC 60601-1-2, IEC/ EN61326-1, IEC/ EN61326-2-6, standards for EMC.

8. Software Verification and Validation Testing

Software verification and validation testing were conducted and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a "moderate" level of concern since there is no direct patient contact, any possible injury to a patient is indirect.

9. Conclusions drawn from Performance Testing

The performance data and information provided in this submission support a substantial equivalence determination for the TEG® 6s Hemostasis System assay cartridges Citrated: K, KH, RTH, FFH and the predicate device K150041 TEG 6s with the Citrated Multichannel Cartridge.

10. Location of Studies

All studies were performed in the United States.

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